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# REMARKS

The above amendment to the specification is submitted for the purpose of bringing the application into accord with regulations governing sequence information in applications. Submitted simultaneously herewith is a Response to a Notice to Correct regarding sequence information, consistent with the application as filed. Consequently, no new matter is introduced through the instant amendment. Entry of the amendment is respectfully requested.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE TO PARAGRAPHS

Please replace paragraph 7 with the following amended paragraph 7:

[0007] In a first embodiment, the present invention provides a pharmaceutical agent comprising a carrier moiety and a therapeutically active peptide species, wherein the peptide is in the form  $aa_n$ , where  $n$  is the number of amino acid residues in the peptide. Preferably, the carrier moiety comprises an aryl or alkyl group of sufficient length or steric bulk to protect the active peptide species from enzymatic degradation *in vivo*. More preferably, the carrier is selected from a group comprising cinnamoyl, benzoyl, phenylacetyl, 3,4-methylenedioxycinnamoyl, 3,4,5-trimethoxycinnamoyl, *t*-butoxycarbonyl, benzyloxycarbonyl, pivaloyl, N-9-fluorenylmethoxycarbonyl, and fumaroyl. Furthermore the carrier moiety can be chemically linked to a therapeutically active peptide species of the general formula  $aa_n$ , where  $n$  is an integer from 2 to 40. In addition, this embodiment of the present invention contemplates a therapeutically active peptide species that is poorly absorbed orally. Preferably,  $n$  is an integer from 3 to 6. More preferably,  $n$  is 5. More preferably still, the therapeutically active peptide species comprises Tyr-Gly-Gly-Phe-Met (SEQ ID NO: 1).

Please replace paragraph 14 with the following amended paragraph 14:

[0014] In one embodiment, the present invention provides a pharmaceutical composition for use in the treatment of physiological conditions comprising a carrier moiety and a therapeutically active peptide species as defined above. The carrier comprises an aryl or alkyl group of sufficient length and/or steric bulk to inhibit rapid enzymatic degradation of the active drug species *in vivo*. A preferred carrier is selected from a group comprising cinnamoyl, benzoyl, phenylacetyl, 3,4-methylenedioxycinnamoyl, 3,4,5-trimethoxycinnamoyl, *t*-butoxycarbonyl, benzyloxycarbonyl, pivaloyl, N-9-fluorenylmethoxycarbonyl, and Fumaroyl. The carrier moiety is chemically linked to a therapeutic polypeptide of the general formula  $aa_n$ , where  $aa$  is an amino acid, or a chemical or structural variation thereof as defined above, where  $n$  is an integer from 2 to 40, and wherein the polypeptide is poorly absorbed orally. Preferably, in the drug composition of the invention,  $n$  is an integer from 3 to 6. More preferably,  $n$  is 5. In a particularly preferred embodiment, the polypeptide is Tyr-Gly-Gly-Phe-Met (SEQ ID NO: 1).<sup>2</sup>

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Please replace paragraph 26 with the following amended paragraph 26:

**[0026]** Met-Enkephalin (Tyr-Gly-Gly-Phe-Met) (SEQ ID NO: 1) is a naturally occurring pentapeptide (n = 5) belonging to the endorphin class. It is known to be involved in the basic mechanisms of analgesia. It produces a transient analgesic effect when administered parenterally, but no effect has been observed when given orally. Its mechanism of action is believed to involve binding to opioid delta receptors in the brain. Met-Enkephalin is very rapidly degraded *in vivo* into a tetra-peptide that is subsequently metabolized. As for the pharmacokinetics of Met-Enkephalin, the plasma levels of the pro-drug, as well of those of the metabolites, are barely measurable, even when administered parenterally.

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